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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/428,458	10/28/1999	KJETIL TASKEN	Q-56244	4681

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EXAMINER
SCHMIDT, MARY M

ART UNIT	PAPER NUMBER
1635	11

DATE MAILED: 12/19/2001

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No. 09/428,458	Applicant(s) TASKEN ET AL.	
	Examiner Mary Schmidt	Art Unit 1635	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on _____ .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *22-24,35,38 and 39* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *22-24,35,38 and 39* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☒ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) *6 & 8* .
4) ☐ Interview Summary (PTO-413) Paper No(s) _____
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

1. Claims 22, 23, 24, 38 and 39 are pending upon entry of the response filed 09/28/01.

Applicant's election with traverse of Group V in Paper No. 10 is acknowledged. However, the restriction is moot in view of the cancellation of claims 25-34 and 36-37. The traversal was on the ground(s) that Groups I and V are not distinct since the claimed analogs of Group V are considered antagonists as broadly categorized in Group I. This is found persuasive, and Groups I and V are rejoined since they encompass the same claims and the dependent claims drawn to other types of antagonists(for instance, ribozymes and antisense) were canceled.

The requirement is still deemed proper and is therefore made FINAL.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention

2. Claims 22, 23, 24, 35, 38 and 39 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

Claim 22 is drawn to a pharmaceutical composition useful for treating an immunosuppressive disease comprising (a) a pharmaceutically effective amount of a cAMP antagonist, wherein said cAMP antagonist selectively or specifically abolishes the function of cAMP dependent kinase (PKA) type Ialpha isozyme ; and (b) a pharmaceutically acceptable adjuvant or filler. Claim 23 further limits the antagonist as a thio-substituted cAMP analog, wherein said thio-substituted cAMP analog is an equatorial dastereomer of 3',5'-cyclic adenosine monophosphorothioate (RP-cAMPS), and wherein said thio-substituted cAMP analog binds to an Rialpha subunit of said isozyme and acts as a selective or specific antagonist of said isozyme. Claim 24 further specifies the cAMP antagonist as selected from the group consisting of Rp-8-Br-cAMPS and Rp-8-Cl-cAMPS. Claim 35 further specifies that the immunosuppressive disease of claim 22 is selected from the group consisting of AIDS, HIV infection and CVI. Claims 22, 23, 24 and 35 thus have an implied use in vivo since pharmaceutical compositions are used for administration to a whole organism. The claims also state that the compositions must function in the treatment of an immunosuppressive disease (in a whole organism).

Claims 38 and 39 are drawn to methods of inhibiting the effects mediated by PKA type Ialpha isozyme comprising administering to subject in need of said inhibition, the pharmaceutical composition of any of claims 22, 23 or 24, so as to inhibit the localization of PKA type Ialpha isozyme with T cell receptor/CD3 complexes. Claim 39 further specifies wherein the subject is afflicted with an immunosuppressive disease selected from the group consisting of AIDS, HIV infection and CVI. Claims 38 and 39 are thus drawn to methods of treatment of any whole

organism subject via administration of pharmaceutical compositions comprising any cAMP antagonist.

The specification as filed, as well as the work by inventors in the post-filing art, teach methods of administration of the Rp-8-Br-cAMPS and Rp-8-Cl-cAMPS to purified T-cells (and specifically from patients having AIDS for instance), and the increased proliferation of T-cells in cells in culture upon such administration. However, neither the specification nor the art teach administration of such compounds to whole organisms for the therapeutic purposes claimed.

There is a high level of unpredictability in the art for *in vivo*, whole organism, treatments of immunosuppressive diseases with therapeutic compounds such as the cAMP antagonists instantly claimed. While the specification and the post-art teach the utility of these Rp-8-Br-cAMPS and Rp-8-Cl-cAMPS in purified T-cells in culture for obtaining the desired novel increase in T-cell production, by having an effect on the PKA type Ialpha isozyme, such results do not correlate to an expectation of similar results in vivo, in a whole organism. Primarily such in vitro results are not reproducible in vivo since in general in vitro cells may be manipulated more easily and higher concentrations of test compounds used than in a whole organism. In a whole organism the entire physiology of the organism necessitates consideration of unpredictable factors such as specific delivery of the pharmaceutical composition to the desired cell types, sustained action of the pharmaceutical, degradation of the pharmaceutical, toxicity of the pharmaceutical, and non-specific interaction of the pharmaceutical. In the instant case, cAMP is an important molecule in every cell of the human body, and delivery of cAMP antagonists would not only effect T-cells as

desired in the present invention, but would effect other cAMP molecules throughout the whole organism, and thus would have an expected effect on other cells in the whole organism, and unpredictable effects not encompassed by the instant invention. Without guidance as to how to localize the effect to a target region, and in an effective concentration, without toxicity, for the treatment effects claimed one skilled in the art would necessarily practice "trial and error" experimentation to make and use the claimed pharmaceutical compositions for use in whole organisms as claimed. Neither the art nor the specification provide such guidance to one skilled in the art. As such, it would necessarily practice undue experimentation to make and use the claimed invention.

Please note that claims 22, 23, 24 and 35 would be free of the 35 U.S.C. 112, first paragraph, enablement rejection, if re-written to claim a composition comprising the antagonist and a pharmaceutically acceptable carrier, for example, instead of a "pharmaceutical composition."

Claim Rejections - 35 USC § 102

3. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless --
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

4. Claims 22, 23, 24 and 35 are rejected under 35 U.S.C. 102(b) as being anticipated by Gjertsen et al. (J. Of Biol. Chem. (1995), 270 (35), 20599-607)

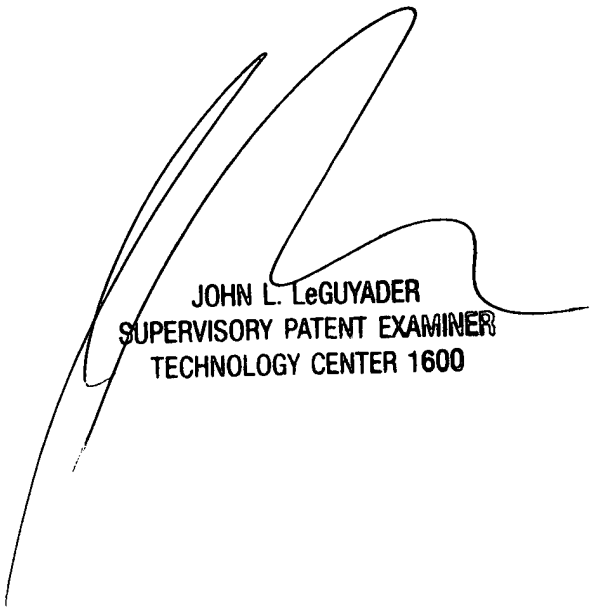
Claims 22, 23, 24 and 35 are drawn to compositions comprising a cAMP antagonist such as a thio-substituted cAMP analog, such as Rp-8-Br-cAMPS and Rp-8-Cl- cAMPS.

Gjertsen et al. teach that the Rp-8-Br-cAMPS and Rp-8-Cl-cAMPS compositions were known at the time the invention was made. Although they do not specifically teach formulation of said compounds into pharmaceutical compositions for treatment of an immunosuppressive disease such as AIDS, HIV infection or CVI, they read on the claimed invention since the claims as written are drawn to the cAMP analog compositions and a pharmaceutically acceptable adjuvant or filler, encompassing the buffers taught by Gjertsen et al. (see page 20600, col. 1, "Experimental Procedures")

Any inquiry concerning this communication or earlier communications from the examiner should be directed to *Mary M. Schmidt*, whose telephone number is (703) 308-4471.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, *John LeGuyader*, may be reached at (703) 308-0447.

Any inquiry of a general nature or relating to the status of this application should be directed to the Group Analyst, *Katrina Turner*, whose telephone number is (703) 305-3413.



M. M. Schmidt
December 17, 2001